

objections, allow Claims 1 to 3, and pass this application to issue.

The courteous interview granted applicant's attorney is gratefully acknowledged.

A number of amendments have been made to avoid the formal rejection. The subject cell line has been identified by its A.T.C.C. accession number and accompanying this response are copies of the letters to and from the A.T.C.C. establishing the deposit of the referenced cell line for patent purposes. So far as the parent cell lines, IL-2 is old, notorious and generally available, and does not require deposit or any additional reference. The line UC729-6 is a cell line which has been deposited in accordance with an earlier filed application, which earlier filed application is properly referenced. Finally, deposit of these earlier cell lines and other identification should not be required, since the subject invention is enabling in providing the subject cell line. As far as applicant's attorney is aware, there is no requirement in providing starting materials to enable someone else to reproduce the cell line, where the cell line itself is available.

Claim 3 has been amended to clarify an apparent ambiguity.

Before discussing the individual references, it is believed warranted to discuss the subject invention. What applicants have done is to greatly enhance the efficiency of fusion as compared to the parent cell line. This is specifically set forth on Page 9, lines 15 to 25.

As far as applicant's attorney is aware, the mechanism for enhanced efficiency is not known. Furthermore, there has been no showing, certainly not in the art cited by the Examiner, that mechanisms have been established for enhancing fusion

interview, the technique employed would appear to be primarily directed to providing cells which do not require the expensive fetal calf serum, but can be grown in a cheaper medium, i.e., Iscove's medium. Also, as was discussed in the interview, there are many alternative media, so that it is not immediately apparent that one should use any particular medium, when trying to wean the cells from fetal calf serum. Thus, the invention is truly serendipitous in having found a cell line with greatly enhanced efficiency.

As discussed in the interview, the Examiner recognized that a thousand-fold improvement is a relevant one. In view of the fact that the subject invention is a substantial advance over the prior cell line, where the advance was obtained by a mechanism which is not at all apparent, it is submitted that the subject cell line is patentably distinct from the prior art.

It would seem that the parent cell line UC729-6 would be the most relevant prior art. This cell line is the cell line which was derived from a myeloma cell line which was modified to become HAT-sensitive. Croce is concerned with a lymphoma line, not a myeloma line, and this is an ample distinction. Even more so, since Croce is concerned with providing a fusogen and not enhancing its hybridization efficiency. Iscove's medium is clearly old. The original cell line, developed by Levy is also admittedly old. However, there is no teaching of the subject invention, which employs growing cells in Iscove's medium to enhance fusing efficiency.

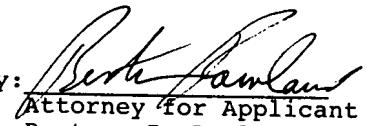
During the interview, it was discussed whether to limit Claim 3 to the fusogen of Claim 1. While at first blush during the interview, this seemed reasonable, after further consideration, it is believed to be unwarranted. The fact is, that while the method finds use in weaning FCS dependent cells

selecting for high fusion frequency. That there is such an opportunity when using Iscove's medium is the gravamen of the subject invention. Without having taught that this method can fulfill a dual purpose, no one would use Iscove's medium to enhance fusion efficiency. If one does not wish to infringe the subject invention, while still wishing to wean a cell line from FCS to Iscove's medium, a high fusion frequency cell line can be developed and then weaned. Therefore, the subject invention does not inhibit reducing a cell line's dependence on FCS, unless this is coupled with the substantial enhancement of fusion frequency.

In view of the above amendments and remarks, and the accompanying documents, the application is considered in good and proper form for allowance, and the Examiner is earnestly requested to withdraw the rejections and pass this application to issue.

Respectfully submitted,

TOWNSEND and TOWNSEND

Date: 6/28/82  
By:   
Attorney for Applicant  
Bertram I. Rowland  
Reg. No. 20,015

BIR:bee

Enclosures: ATCC Letter dated April 8, 1981  
(Documents) ATCC Letter dated April 26, 1981

1510262482200

LAW OFFICES  
TOWNSEND AND TOWNSEND

PATENTS, TRADEMARKS, AND COPYRIGHTS

STEPHEN S. TOWNSEND  
ANTHONY B. DIEPENBROCK  
DIRKS B. FOSTER  
THOMAS F. SMEGAL, JR.  
WILLIAM MICHAEL HYNES  
BERTRAM I. ROWLAND  
BRUCE W. SCHWAB  
WARREN P. KUJAWA  
ROBERT J. BENNETT  
HENRY C. BUNSWO  
SANDRA S. SCHULTZ  
JAMES F. HANN  
JAMES M. HESLIN

CHARLES E. TOWNSEND, JR.  
ALBERT J. HILLMAN  
JOHN L. McGANNON  
PAUL W. VAPNEK  
J. GEORG SEKA  
ROGER L. COOK  
RONALD SHELDON LAURIE  
GEORGE M. SCHWAB  
KENNETH R. ALLEN  
DAVID N. SLONE  
LESLEY S. WITT  
ROBERT C. COLWELL

MARK MOHLER  
J. THOMAS McCARTHY  
OF COUNSEL

TWENTIETH FLOOR  
STEUART STREET TOWER  
ONE MARKET PLAZA  
SAN FRANCISCO, CALIFORNIA 94105  
(415) 543-9600  
CABLE "DEWEY"  
TWX  
910-372-6566  
TOWNSEND SFO

PALO ALTO OFFICE  
NUMBER FIVE PALO ALTO SQUARE  
3000 EL CAMINO REAL  
PALO ALTO, CALIFORNIA 94304  
(415) 493-2590

CHAS E. TOWNSEND (1904-1944)

April 8, 1981

American Type Culture Collection  
12301 Parklawn Drive  
Rockville, Maryland 20852

Attention: Ms. Bobbie Brandon

Re: HIGH FUSION FREQUENCY FUSIBLE  
LYMPHOBLASTOID CELL LINE  
Our File No.: 2307U-107 (UC 205-80)

Dear Ms. Brandon:

Submitted herewith are the forms for deposit of  
W1-L2-729 HF<sub>2</sub> human lymphoblastoid B-cell line. The W1-L2-729-  
HF<sub>2</sub> is being forwarded under separate cover in  
No. and container \_\_\_\_\_ on (already sent).

ATC  
CR1 0062

This deposit is being made by the undersigned  
on behalf of Robert L. Lundak and The  
Regents of the University of California ("Regents") to whom  
United States and foreign patent rights have been or will be  
assigned. Since this deposit is being made in connection with  
the filing of (X) United States and ( ) foreign patent applications,  
it is on a restricted basis. The deposit should be maintained for  
patent purposes for 20 years, and please bill us for the appropriate amount.

TERMS AND CONDITIONS OF DEPOSIT

The following terms and conditions are hereby specified as the contract of deposit for W1-L2-729-HF.

(1) The deposit is on a restricted basis, the restrictions are subject to the ruling set forth in *In re Argoudelis et al*, 168 USPQ 99 (CCPA 1970). During the pendency of the

restricted maintenance of the deposit, which will end on the date of the earlier of the publication of a foreign patent or patent application requiring that the deposit be made available under restricted circumstances or the issuance of a United States Patent referring to the subject deposit, A.T.C.C. agrees to protect the confidentiality of the deposit as follows:

(a) A.T.C.C. shall not reveal the possession of the deposit, any characteristics of the deposit, nor the source of the deposit.

(b) The deposit shall be held and used solely for storage and maintenance. Any activities with the deposit shall be limited to the maintenance of the deposit and assurance of the continued viability of the deposit.

(c) Except under express written authorization from the depositor or Regents, no one shall be permitted by A.T.C.C. to do any studies of the deposit or excretory products of the deposit and any media in which the deposit is grown shall be promptly destroyed after having served its nutrient function. All copies of the deposit other than those maintained for storage shall likewise be destroyed.

(2) The release of the restricted condition of deposit and all other matters relating to the deposit shall be the responsibility of The Regents of the University of California, as represented by Roger G. Ditzel, Patent Administrator. All communications concerning this deposit should be directed to Mr. Ditzel at Office of the Board of Patents, 491 University Hall, 2200 University Avenue, Berkeley, California 94720. Mr. Ditzel's telephone number is (415) 642-5000.

(3) The Regents of the University of California through Mr. Ditzel will advise A.T.C.C. whenever the allowance, publication, or issuance of a United States or foreign patent which relates to this deposit requires the release of the restricted condition of deposit. Should the deposited culture die or be destroyed during the effective life of any such patent, The Regents of the University of California will have the responsibility for replacing it with a living culture of the deposit.

(4) Consent is given in advance that said deposit during the pendency of any United States patent application relating thereto, may be made available on order of the United States Commissioner of Patents and Trademarks, pursuant to Rule 1.14 of the Rules of Practice in Patent Cases, and 35 U.S.C. 122.

Page Three (3)

(5) In the event that at a future date there is no pending patent application or issued patent in the United States or in a foreign country requiring this deposit to be maintained, it is understood that on request the A.T.C.C. will return the deposit on being advised of this fact and so requested by or on behalf of The Regents of the University of California.

To facilitate the immediate filing of a United States patent application, we would appreciate prompt assignment of an A.T.C.C. number. A telephone call to Mr. Rowland at the above number in Palo Alto will be appreciated. All correspondence should be sent to the Palo Alto address to my attention. All bills should be sent to the San Francisco address to the attention of Ms. Kathy Krause.

Thank you very much for your cooperation in this matter.

Very truly yours,

TOWNSEND and TOWNSEND



Bertram I. Rowland

BIR/sb  
cc: Roger G. Ditzel

UNDERSTOOD AND AGREED:

By: Bobbie A. Brandon

Date: April 13, 1981



# American Type Culture Collection

23070-107

12301 Parklawn Drive, Rockville, Maryland 20852 USA 301-881-2600 Telex ATCCROVE 908-768

Since 1925  
an independent non-profit  
organization incorporated in  
Washington, D.C. and devoted to  
the preservation of reference  
cultures and their distribution to  
the scientific community

*(initials)*  
8/11/82

#### AFFILIATED ORGANIZATIONS:

American Association of Immunologists

American Institute of Biological Sciences

American Phytopathological Society

American Society of Biological Chemists

American Society for Microbiology

American Society of Parasitologists

American Society of Zoologists

American Society of Tropical Medicine and Hygiene

Genetics Society of America

Infectious Diseases Society of America

Mycological Society of America

National Research Council-National Academy of Sciences

Society of Protozoologists

Tissue Culture Association

The American Type Culture Collection (ATCC) has received your deposit of a culture in connection with the filing of an application for a patent. The following information is provided to fulfill the Patent Office requirements.

Name and Address of Depositor:

Mr. Bertram I. Rowland, Esq.  
Townsend and Townsend  
5 Palo Alto Square  
Palo Alto, California 94304

On behalf of

Dr. Robert L. Lundak and the Regents of the University of California, Riverside

Date of Receipt of Cultures by the ATCC: 4-2-81

<u>Scientific Description</u>	<u>Depositor's Reference</u>	<u>ATCC Accession Number</u>
Human lymphoblastoid B-cell line	W1-L2-729 HF <sub>2</sub>	CRL 8062

The ATCC understands that:

1. The deposit of this culture does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied, to infringe the patent, and our release of this culture to others does not grant them a license, either expressed or implied, to infringe the patent.
2. If this culture should die or be destroyed during the effective life of the patent it shall be your responsibility to replace it with a living culture of the same organism. It is also your responsibility to supply a sufficient quantity for the period of storage specified below.

The ATCC agrees that in consideration for a one-time service charge, not to distribute this culture or any information relating thereto or to its deposit until such time as a patent has been issued disclosing the above deposit except in accordance with U. S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make this strain available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the culture for a period of 20 years from the deposit date. Nonpayment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

American Type Culture Collection

Date: April 26, 1981

By: Bobbie A. Brandon  
(Mrs.) Bobbie A. Brandon, Head  
Professional Services Department

cc: Mr. Roger G. Ditzel  
Patent Administrator

Ms. Kathy Krause  
Townsend and Townsend